Behavioral Disconnection Syndrome Manifesting as Combined Mania and Visual-Auditory Hallucinations Secondary to Isolated Right Thalamic Hemorrhage

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Damage to the thalamus can contribute to the phenomenon of diaschisis manifesting as various behavioral symptoms. We present the case of a 55-year-old man who presented with acute mania and late-onset combined visual and auditory hallucinations after right thalamic hemorrhage. This is the first report, to our knowledge, of a combination of mania and visual-auditory hallucination in a patient with isolated thalamic damage. Details of all previous case reports on isolated thalamic damage presenting with mania or hallucination are provided. We propose the networks of diencephalic damage causing mania and hallucinations, which represent the behavioral disconnection syndromes.

It is challenging to localize a single lesion when neuropsychiatric symptoms are the only manifestations. The thalamus is a complex structure connecting between the brainstem and various cortical areas. Damage to the thalamus can contribute to various behavioral conditions. We report the first case, to our knowledge, of a patient who suffered from right thalamic hemorrhage presenting with combined acute mania and visual-auditory hallucinations. The case broadens the clinical approach on the behavioral disturbance secondary to focal brain lesion on the thalamus. We also systematically review the previous reports on the cases of isolated thalamic damage with mania or hallucination. Finally, we provide the proposed networks of diencephalic damage causing mania and hallucinations.

CASE REPORT

A 55-year-old man without a previous history of psychiatric conditions or substance abuse presented with a 1-week history of acute mania. He had irritability, grandiosity, combative speech, paranoid delusion, high energy levels, decreased need for sleep, pressurized speech, euphoria, and inappropriate cheerfulness. The patient had been a mild-mannered and composed person prior to this event. Neurological examination showed no focal neurologic deficits; urine drug screen was negative; MRI showed cavernous malformation with hemorrhage involving the dorsomedial and pulvinar nucleus of the right thalamus (Figure 1); and electroencephalography was normal. Risperidone was started. At 4 months follow-up, the manic symptoms resolved, and risperidone was discontinued.

One year later, he presented with acute psychosis. He had vividly visual hallucination (transient texts on his phone, unknown people and colorful airplanes). He also reported the musical hallucination that he heard pleasant classical music in particular at night. He denied any commanding or voice hallucination. He had hypnagogic visual and musical hallucinations. He has insight to the hallucinations. MRI head demonstrated stable cavernous malformation (Figure 1). Risperidone was resumed and effectively improved hallucination within a week.

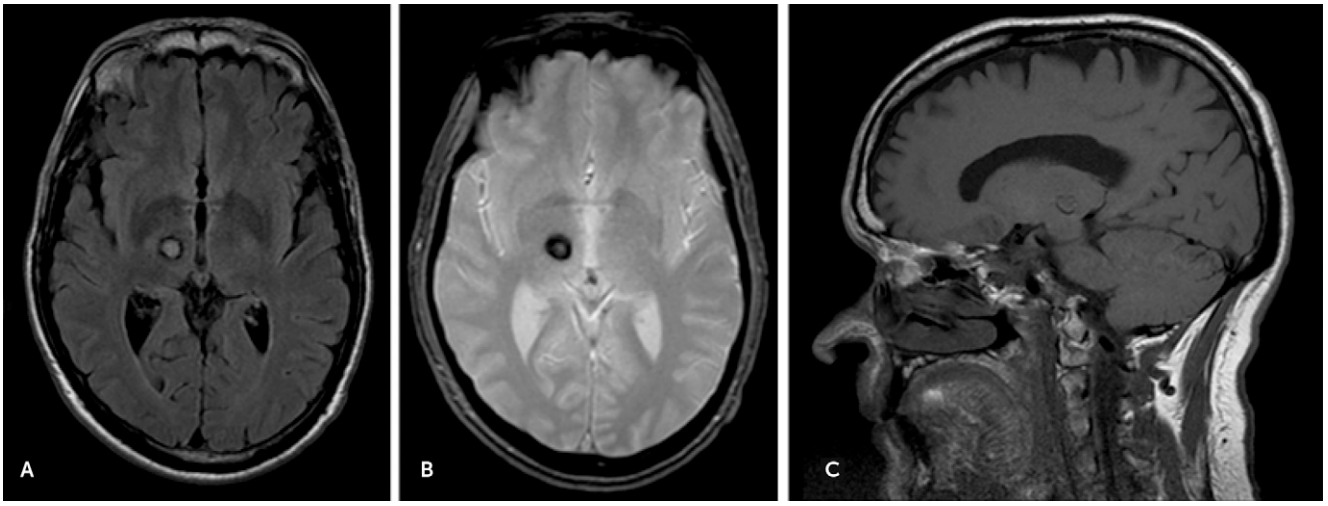
DISCUSSION

Mania

Mania after thalamic lesions has been described in a small number of patients. Symptoms of mania secondary to focal brain lesions are clinically similar to the features of primary psychiatric mania. Some features may help localizing lesions to the thalamus or differentiating from primary mania, such as hemianesthesia, hemiparesis, hypersomnolence, abnormal movement, abnormal gaze, and amnesia.

From literature review, we found 18 cases of mania (including our case) caused by isolated thalamic lesions on various thalamic nuclei, including the dorsomedial, intralaminar, pulvinar, anterior, ventrolateral, and ventromedial nuclei (Table 1). It is interesting that, in all of these cases, the lesions involved the right thalamus, with the isolated right thalamus in 72% (N=13/18) of cases and both thalami in 28% (N=5/18) of cases. The majority of patients (80%) developed mania immediately or within a few days after the damage; however, late-onset mania may occur up to many months after the events. In cases with mild symptoms, patients usually spontaneously recover without medication. In more severe cases, mood stabilizers or atypical antipsychotics are effective treatment. Even though most of the reported patients did not have recurrent mania, a minority of the cases developed hypomania or cyclic depression-mania during the follow-up period.

FIGURE 1. MRI Head Showing the Cavernous Malformation Hemorrhage on the Right Thalamus Involving the Dorsomedial and Pulvinar Nuclei[a]



[a] The image shows A) axial view on the fluid-attenuated inversion recovery sequence; B) axial view on the gradient-echo sequence; and C) sagittal view on the T1 sequence.

Peduncular Hallucinosis

Peduncular hallucinosis classically presents with vivid visual hallucination usually with preserved insight. Midbrain damage with or without thalamic involvement is the typical origin of hallucination. Isolated thalamic lesions were rarely reported to cause this condition (Table 2). From the literature review, we found 15 cases (including our case) of hallucinations secondary to isolated thalamic damage. Even though there is no specific thalamic nucleus consistently reported to cause peduncular hallucinosis, the dorsomedial (46%, N=6/13 cases), pulvinar (31%, N=4/13 cases), and anterior (15%, N=2/15 cases) nuclei are the common locations contributing to this condition (Table 2). Unlike mania, there is no relationship between the side of diencephalic lesions and hallucinations. From 15 case reports, the lesions were on the right side in 47% (N=7/15 cases), on the left side in 47% (N=7/15 cases), and on both sides in 6% (N=1/15 case). Similar to mania, the majority of peduncular hallucinosis (66%, N=10/15 cases) occurred within the first week after damages, but late-onset can present up to a year as reported in our case. Atypical antipsychotics are the drug of choice in severe cases.

Even though visual hallucination is the classic type of peduncular hallucinosis, auditory hallucinations also occur after diencephalic damage. To our knowledge, there have been only two case reports of combined visual and auditory hallucinations secondary to isolated thalamic lesions, which involved the anterior and lateral nuclei in each case. Our case is the first report of damage to the dorsomedial and pulvinar nuclei contributing to combined hallucinations.

Network Model of Mania and Hallucinations Secondary to Thalamic Insults

Mania secondary to diencephalic lesions derives from the phenomenon of diaschisis that is caused by disconnection of the thalamus from the thalamo-prefrontal-limbic networks. The magnocellular (medial) part of the dorsomedial nucleus connects the thalamus with the limbic system via the orbitofrontal cortex.[1] Damage to this network causes disinhibition of inappropriate behaviors and enhanced reward-seeking behaviors.[2] The medial part of the dorsomedial nucleus also projects the neuronal network to the amygdala via the amygdalofugal tract, and thus a lesion on this nucleus can lead to emotional dysregulation, aggression, increased oral intake, and hypersexuality. In addition, damage to the intermediate part of dorsomedial nucleus, which links to the dorsolateral prefrontal cortex, can contribute to executive dysfunction.

Damage to the anterior nucleus, which is connected to the mammillary bodies and amygdala via the mamillothalamic and ventral amygdalothalamic tract, respectively, causes problem with emotional expression and dysregulation of motivation.[1] The pulvinar nucleus is an associative nucleus connecting to multiple cortical areas.[1] The medial part of the pulvinar nucleus sends some connections to the anterior insular cortex and functions in controlling emotional awareness that is required for emotional regulation.[3] Some fibers from the intermediate part of the pulvinar nucleus also project to the dorsolateral prefrontal cortex and take part in executive performance.

The role of the right thalamus in the pathogenesis of mania is supported by previous studies demonstrating decreased right thalamic volume in patients with bipolar disorder compared with normal controls[4,5] and reduced right thalamic and ipsilateral prefrontal/orbitofrontal perfusion in cases with diencephalic mania.[6–8] It is hypothesized that emotional regulation is lateralized, with the right hemisphere controlling negative moods and the left hemisphere controlling positive emotions. The interhemispheric imbalance, with left-sided hyperfunction and right-sided hypofunction, on the prefrontal, orbitofrontal, and insular cortices, may contribute to the emotional releasing effect from the contralesional side and result in secondary mania.[9,10]

TABLE 1. Cases With Isolated Thalamic Damage Causing Mania

Study	Sex	Age (Years)	Locations	Hemisphere	Onset	Etiologies	Manic Symptoms	Associated Symptoms	Treatment
Cummings et al.[13]	Two cases	NA	Unspecified	Right	Acute	Ischemic stroke	Case 1: euphoria, talkativeness, hypersexuality, euphoric, irritable, and poor judgement Case 2: euphoric, decreased need for sleep, and preoccupied with religion	Hemisensory loss, amnesia, denial of illness, and depression (case 2)	Lithium in one case with improvement; no medication in one case
Gentilini et al.[14]	Male	66	Paramedian	Right and Left	Acute	Ischemic Stroke	Hypersexuality, grandiosity, and cheerfulness	Amnesia, somnolence, and delusion	Not reported
	Female	47	Paramedian	Right and Left	Acute	Ischemic stroke	Hyperphagia, euphoria, and childish behaviors	Hypersomnolence, abnormal eye movement, and depression	Not reported
	Male	35	Paramedian	Right and Left	Acute	Ischemic stroke	Hyperphagia and irritability	Amnesia	Not reported
Bogousslavsky et al.[6]	Female	72	Paramedian, dorsomedial and ventral lateral	Right	Acute	Ischemic stroke	Smiling and inappropriate laughing and jokes, logorrhea, rapid switching of ideas, lack of spontaneity, and disinhibition	Hypersomnolence, disorientation,	Not reported
Starkstein et al.[15]	Three cases	NA	Unspecified	Right	NA	Hemorrhage and ischemic stroke	Mania (unspecified symptoms in each case)	NA	NA
Kulisevsky et al.[16]	Female	81	Ventral lateral and ventromedial	Right	Acute	Ischemic stroke	Euphoria, talkativeness, grandiosity, flight of ideas, inappropriate jokes, and decreased need for sleep	Left hemichorea	Haloperidol with improvement after 4 weeks
McGilchrist et al.[17]	Male	43	Paramedian	Right and Left	Acute	Ischemic stroke	Cyclic elation, hypersexuality, hyperphagia, flight of ideas, and decreased need for sleep	Hypersomnolence, cyclical apathy and depression	Not reported
Daum et al.[18]	NA	64	Anterior	Right	Acute	Ischemic Stroke	Hypersexuality, talkativeness, irritability, mood fluctuation, and verbal aggression	Amnesia	Not reported

continued

TABLE 1, *continued*

Study	Sex	Age (Years)	Locations	Hemisphere	Onset	Etiologies	Manic Symptoms	Associated Symptoms	Treatment
Vuilleumier et al.[19]	Male	63	Unspecified	Right	Acute	Ischemic stroke	Mania episode followed by hypomania	Prosopoaffective agnosia	Not reported
Leibson[20]	Male	53	Unspecified	Right	Acute	Hemorrhage	Talkativeness, cheerfulness, hypersexuality, and increased energy	Anosognosia, headache and left-sided numbness and weakness, gaze problem, and hemineglect,	Resolved 10 weeks after the stroke
Inzelberg et al.[21]	Male	61	Pulvinar	Right	Acute	Ischemic stroke	Euphoria, talkativeness, disinhibition, flight of ideas, hypersexuality, decreased need for sleep, and increased goal-directed activity	Left hemichorea	Haloperidol with improvement after 8 weeks
Benke et al.[7]	Male	38	Dorsomedial, intralaminar and anterior	Right and Left	4 weeks	Ischemic stroke	Logorrhea, restlessness, mood elevation, inflated self-esteem, reduced need for food and sleep, and hypersexuality	Amnesia, vertical gaze paralysis, and dysarthria	Low-dose neuroleptic with improvement after 8 weeks
Lopez et al[8]	Male	63	Unspecified	Right	5 months	Ischemic stroke	Cyclic mania	Bipolar symptoms with cyclic depression, and melancholic stupor	Risperidone, valproic acid, and quetiapine for mania
Routh and Hill[22]	Male	83	Posterior	Right	2 weeks	Hemorrhage	Aggressiveness, speech disinhibition, talkativeness, flight of ideas, and inflated self-esteem	Paranoid delusions	Olanzapine
Julayanont et al. (current case)	Male	55	Dorsomedial and pulvinar	Right	Acute	Hemorrhage	Irritability, grandiosity, combative speech, high-energy levels, decreased need for sleep, pressurized speech, euphoria, and inappropriate cheerfulness	Paranoid delusions and amnesia	Risperidone with improvement after 4 weeks

TABLE 2. Cases With Isolated Thalamic Damage Causing Hallucinations

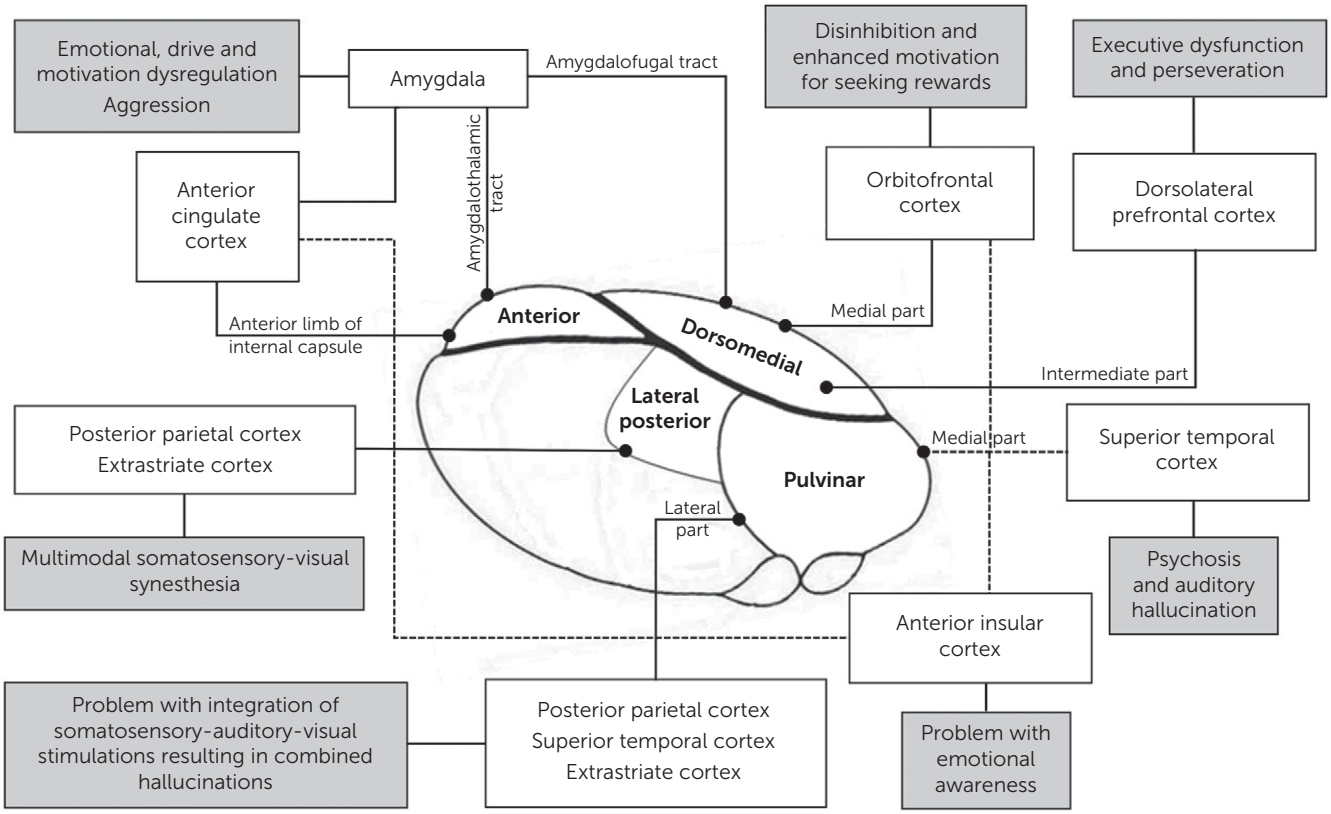
Study	Sex	Age (Years)	Locations	Hemisphere	Etiologies	Onset	Hallucination Features		Associated Symptoms	Treatment
							Visual	Auditory		
Feinberg and Rapcsak[23]	Male	83	Dorsomedial	Right	Ischemic stroke	Acute	Animals in his house (flying birds and dogs), military marching, girls in an examination room	No	Vertigo, ataxic gait	Resolved in 1 week
Serra et al.[24]	Male	68	Posterior	Right	Ischemic stroke	Acute	Animals and men's head	No	Left hemiparesis, paraesthesias	Not reported
Inzelberg et al.[25]	Female	75	Unspecified	Left	Ischemic stroke	2–3 days	No	Musical hallucination of popular songs from her youth	Right hemiparesis and dysphasia	Improved with no reported treatment
Noda et al.[26]	Male	72	Dorsomedial	Right	Ischemic stroke	3 days	Vivid recollection of his old job, dish of sweet potatoes and cigarette between his fingers	No	Hypersomnolence and nocturnal insomnia	Resolved over 2 weeks with no reported treatment
	Female	46	Anterior	Left	Ischemic stroke	4 days	Parents who passed away 10 years ago, teapot and teacups on a table	Commanding voice: "Don't eat"	Memory impairment, right upper limb weakness	Resolved over 2 weeks with no reported treatment
Manford and Anderson[27]	Male	58	Pulvinar	Right	Ischemic stroke	10 days	Ball of light, a man in a suit, a black butterfly, dwarves, striped fish swimming	No	No	Not reported
Yoshida et al.[28]	Female	73	Dorsomedial	Left	Ischemic stroke	2 months	No	Voices telling her about misfortunes, voices of threats and commands,	Anterograde and retrograde amnesia	Risperidone and olanzapine

continued

TABLE 2, *continued*

Study	Sex	Age (Years)	Locations	Hemisphere	Etiologies	Onset	Hallucination Features		Associated Symptoms	Treatment
							Visual	Auditory		
Mollet et al.[29]	Female	61	Lateral	Right	Ischemic stroke	Acute	College-age boys in colorful Hawaiian shirts, men in black religious clothes	Conversation between college boys	Pain and numbness at the left hemibody	Not reported
Güzelcan et al.[30]	Male	46	Unspecified	right	Tumor	Not reported	Parades of people, seeing spiders, mice running	No	No	Risperidone
Mittal and Khan[31]	Female	19	Ventroanterior	Left	Ischemic stroke	Acute	No	Commanding Voices	Confusion, flat affect, imaginary boyfriend, and paranoid delusion	Risperidone
Lee et al.[32]	Male	20	Anterior	left	Ischemic stroke	Acute	Dangerous hands and snakes	No	Amnesia, anomia, and depersonalization	Not reported
Fornazzari et al.[12]	Male	45	Lateral and posterior	Left	Hemorrhage	9 months	Sound-tactile, sound-color, and grapheme-gustatory synesthesias		No	Not reported
Delgado and Bogousslavsky[33]	Male	61	Dorsomedial	Left	Ischemic stroke	Acute	Body distortion above the waist, lights and mice running down the wall	No	Transient perioral and left paresthesias	Disappeared without treatment
	Female	48	Paramedian	Right and Left (right >left)	Ischemic stroke	Acute	No	Voice and noise distortion made by "dinosaurs"	Disorientation	Disappeared without treatment
Julayanont et al. (current case)	Male	55	Dorsomedial and pulvinar	Right	Hemorrhage	12 months	Transient texts on his phone, unknown people and colorful airplanes	Musical hallucination	Paranoid delusions and amnesia	Risperidone

FIGURE 2. Proposed Network of Mania and Peduncular Hallucinosis Secondary to Thalamic Lesions



Similar to mania, the diaschisis of neural networks also explains the pathogenesis of peduncular hallucinosis. In the classic peduncular hallucinosis from mesencephalic lesions, the disruption along the pathway from the ascending reticular activating system in the brainstem to the thalamus may contribute to the hallucinations. While in the cases with thalamic lesions, dysregulation between the thalamus and the extrastriate cortex and superior temporal gyrus leads to visual and auditory hallucination, respectively. This hypothesis is supported by a study on the lesion-based resting-state networks, which showed the maximal network overlap for visual hallucinations on the extrastriate visual cortex and for auditory hallucinations on the superior temporal gyrus.[11]

The pulvinar nucleus is the multimodal integrative nucleus connecting to the posterior parietal, superior temporal, and extrastriate cortices. Damage to this structure may also cause problems with somatosensory-auditory-visual integration, resulting in multimodal hallucinations. The lateral posterior nucleus was reported to cause multimodal somatosensory-visual-auditory-gustatory synesthesia.[12]

We propose the network explaining the pathogenesis of mania and peduncular hallucinosis secondary to thalamic lesions (see Figure 2).

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